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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
BAUM, STUART F	

ART UNIT	PAPER NUMBER
1638	

DATE MAILED: 03/21/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/740,582	NIU, MAN C.	
	Examiner	Art Unit	
	Stuart Baum	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-25 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-25 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

Double Patenting

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

Claims 16 and 21 are rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 1-2 of prior U.S. Patent No. 6198025. This is a double patenting rejection.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-15, 19-20, 22, and 25 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific asserted utility, a credible asserted utility or a well established utility.

The inventors claim a method for producing transgenic plants and kernels which express beneficial exogenous proteins, a method for producing transgenic corn plants and kernels expressing soy globulin protein, and a transgenic plant, corn plant and kernels expressing beneficial exogenous proteins produced by a method comprising isolating and purifying soy globulin mRNA from soy sprout, microinjecting 1μg/μl of said purified mRNA into said seed , germinating said seed and growing transgenic corn plants from said seed.

The specification only discloses isolating total RNA from soybeans, either cotyledons or sprouts and isolating polyA RNA by oligo DT chromatography. The mRNA thus isolated was adjusted to 1μg/μl concentration and 1μl of resulting solution was injected separately into imbibed kernels of corn. Injected seeds were planted in rows and allowed to grow to maturity. A total of 134 samples were analyzed from the mRNA-treated group with 29 samples purportedly being transformed. Determination of transformation was by the presence of an additional band on a protein gel when compared to the control group (seeds not injected with RNA). The proteins were extracted from an ear's worth of seeds. The Applicants also performed a Ouchterlony double agar diffusion test using an anti-soy protein serum and a Southern hybridization assay using labeled soy specific probes.

Based on the presented figures, the results from the protein gel, Western blot and Southern hybridization are not convincing. In figure 1, it is not clear if the specified protein band is absent from the control lane. The specificity of the antibody for soy globulin is not

demonstrated in figure 5, which presents a number of protein bands reacting with the antibody serum. The figure legend for figure 6 does not explain the differences between the various lanes nor what the presented band represents and how it was prepared.

A credible asserted utility is not established because the facts upon which the assertion is based are inconsistent with current scientific dogma. Hansen et al (1999, Trends in Plant Science, 4(6) :226-231) teach "Successful transformation of plants demands that certain criteria be met. Among the requirements for transformation are: An efficient DNA delivery method" (page 227, right column, 2nd paragraph). Hansen et al continues by stating that there are a number of techniques for delivery of DNA to host cells; *Agrobacterium*-mediated transformation, biolistic or microprojectile bombardment, electroporation, polyethylene glygol treatment, or liposome treatment (page 228, left column, 2nd paragraph). Songstad et al (1995, Plant Cell, Tissue and Organ Culture 40 :1-15) teach that because of the inherent properties of plant cells, they are not amenable to microinjection as are animal cells because plant cells have a cell wall composed of thick layers of cellulose and lignin that are difficult for a glass microneedle to penetrate and plant cells vacuoles contain many hydrolases and toxic compounds that will kill a cell if the integrity of the vacuole is compromised (page 10, right column, 3rd paragraph). Due to the position of the embryo proper within the seed and the location of the meristem within the embryo, many cell layers have to be traversed by the microneedle which ruptures cells and cell vacuoles and releases hydrolases.

For one skilled in the art, there are a number of inconsistencies which bring into question the credible asserted utility. The specification discloses that total polyA was injected into the corn kernels but that only the soy globulin protein was present on all protein gels analyzed. The

inventor does not teach how to express only one beneficial protein but rather how to express the putative soy globulin protein. In addition, the inventor does not address what precautions must be taken to avoid RNA degradation by RNases which are ubiquitous. Lastly, the inventor does not teach how the corn kernels generate DNA which is supposedly integrated into the host genome from a RNA template; producing only one species of DNA from the population of RNA molecules isolated from the soy plant. As the inventor discloses in the specification, reverse transcriptase is used to generate cDNA (page 11, line 6) which transcribes all mRNA in the reaction. For one skilled in the art, it is not taught from where the reverse transcriptase originates and how one generates only one species of DNA from a population of mRNA.

The method proposed by the inventor comprises promoter-less nucleic acids encoding proteins which is analogous to the gene trap method taught by Babiychuk et al (1997, Proc. Natl. Acad. Sci. 94:12722-12727) in which the promoter-less NPTII gene (neomycin phosphotransferase II which confers Kanamycin-resistant phenotypes) is transformed into Arabidopsis. Babiychuk et al teach that expression of the NPTII gene only occurs when the NPTII gene is integrated into the expressed regions (coding regions) of the *Arabidopsis* genome (page 12723, right column, 1st paragraph). Gai et al (2000, Nucleic Acid Research 28(1) :94-96) teach the genome of corn comprises 50,000-80,000 genes in ~2.3 x 10^9 base pairs present on 10 chromosomes. The average base pair length of a gene is ~3 Kb which translates into 240,000Kbp's of corn genome that is partitioned into genes. The percent of corn genome designated as coding regions equals ~1% [240,000Kbp's of coding region/23,000,000 Kbp's of total DNA]. The inventor claims to have selected 29 transformed T1 plants from 134 kernels treated with mRNA (page 14, line 9). For the inventor to have selected 29 transformed corn

plants, given the genome size and low percentage of DNA allocated to coding regions, the inventor would have to initially treat 2900 corn kernels with mRNA [(the initial number of treated corn kernels) = (the transformed kernels, 29) x (100)].

Therefore, given that plant transformation requires an efficient DNA delivery system and requires that either an *Agrobacterium*-mediated transformation, biolistic or microprojectile bombardment, electroporation, polyethylene glygol treatment, or liposome treatment be used for plant transformation, given the inherent problems with using a glass microneedle when delivering a nucleic acid into a meristem of a corn seed embryo, given the inconsistencies of using the disclosed method to transform a plant using isolated total mRNA and only seeing one protein band on a gel, given the number of putatively transformed plants out of a total number of only 134 corn kernels initially treated with mRNA compared to the expected number of initially treated corn kernels, the credibility of the Applicants specified utility for their invention is not supported in their specification.

Claims 1-15, 19-20, and 25 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a credible asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Claims 1-15, 19-20, and 25 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 1-15, 19-20, and 25 are broadly drawn to a method for producing transgenic plants and kernels which express beneficial exogenous proteins, including a method for producing transgenic corn plants and kernels expressing soy globulin protein, and a transgenic plant, corn plant and kernels expressing beneficial exogenous proteins produced by a method comprising isolating and purifying soy globulin mRNA from soy sprout, microinjecting 1μg/μl of said purified mRNA into said seed , germinating said seed and growing transgenic corn plants from said seed.

Given the unpredictability of producing a plant transformed with mRNA including a corn plant, for the reasons stated above; given the lack of credible working examples of producing a transformed plant from mRNA isolated from another organism as stated above, given the lack of guidance in the specification for producing a transformed plant using mRNA as stated above; and given the absence of working examples that address all of the arguments against using mRNA and seed incubation or microinjection to transform a plant, and given the breadth of the claims, which are drawn to expressing any exogenous protein in any plant by incubating a seed with a RNA, it would require undue experimentation by one skilled in the art to practice the claimed invention.

Claims 11-15, 17-20, and 22-25 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Since the microbe claimed is essential to the claimed invention, it must be obtainable by a repeatable method set forth in the specification or otherwise be readily available to the public. If

a microbe is not so obtainable or available, the requirements of 35 U.S.C. 112 may be satisfied by a deposit thereof. The specification does not disclose a repeatable process to obtain the exact same microbe in each occurrence and it is not apparent if such a culture is readily available to the public. It is noted that applicants have deposited cultures for under the depository accession numbers: NCIMB 40582, but there is no indication in the specification as to public availability. If the deposit of these cultures is made under the terms of the Budapest Treaty, then an affidavit or declaration by the applicants, or a statement by an attorney of record over his or her signature and registration number, stating that the cultures will be irrevocably and without restriction or condition released to the public upon the issuance of a patent would satisfy the deposit requirement made herein.

If the deposit has not been made under the Budapest Treaty, then in order to certify that the deposit, meets the criteria set forth in 37 CFR 1.801-1.809, applicants may provide assurance of compliance by an affidavit or declaration, or by a statement by an attorney of record over his or her signature and registration number showing that

(a) during the pendency of the application, access to the invention will be afforded to the Commisioner upon request;

(b) all restrictions upon availability to the public will be irrevocably removed upon granting of the patent;

(c) the deposit will be maintained in a public depository for a period of 30 years or 5 years after the last request or for the enforceable life of the patent, whichever is longer;

(d) the viability of the biological material at the time of deposit will be tested (see 37 CFR 1.807); and

(e) the deposit will be replaced if it should ever become inviable.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 5, 6, and 8-9 and all subsequent dependent claims are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 and 9 are indefinite for reciting "beneficial" to describe exogenous proteins. It is vague and unclear what characteristics are encompassed by the word "beneficial".

Claims 1 and 9 are indefinite for failing to specifically indicate if the mRNA sample is a heterogenous mixture of mRNA's encoding many proteins other than said exogenous proteins or if mRNA sample is a homogenous solution of just mRNA's encoding said exogenous proteins.

Claim 5 is indefinite for not having an antecedent basis in claim 1 for detecting an exogenous protein.

Claim 6 is indefinite for not having an antecedent basis in claim 1 for "introducing mRNA" into seeds. Claim 1 only recites "incubating seed" with mRNA.

Claim 8 is indefinite because it is unclear if said sprouts are just growing shoots or if this term includes seeds.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stuart Baum whose telephone number is (703) 305-6997. The examiner can normally be reached on Monday-Friday 8:30AM – 5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on (703) 306-3218. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 305-3014 or (703) 305-3014 for regular communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the legal analyst, Kim Davis, whose telephone number is (703) 305-3015.

Stuart Baum Ph.D.

March 11, 2002

ELIZABETH F. McELWAIN
PRIMARY EXAMINER
GROUP 1600